PAPULOSQUAMOUS DISEASES

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Papulosquamous diseases

are those in which the primary lesions typically consist of papules with scale

The category of papulosquamous disease classically includes :

-Psoriasis

-Lichen planus

-Pityriasis rosea

-Seborrheic dermatitis

-Pityriasis rubra pilaris

-Secondary syphilis

-discoid lupus erythematosus,

-Ichthyosis-

-Miscellaneous (mycosis fungoides,) -

Psoriasis

Prevalence

- Psoriasis occurs in 2%(1-3%) of the world's population
- Equal frequency in males and females
- May occur at any age from infancy to the 10th decade of life
- First signs of psoriasis
  - Females mean age of 27 years
  - Males mean age of 29 years

Prevalence

- Two-thirds of patients have mild disease
- One-third have moderate to severe disease
- Early onset (prior to age 15)
  - Associated with more severe disease
  - More likely to have a positive family history
- Life-long disease
  - Remitting and relapsing unpredictably
  - Spontaneous remissions of up to 5 years have been reported in approximately 5% of patients

Etiology

- The cause of Ps. is still unknown
- The course of Ps. is inconstant
- Tendency to recur and to persist
- Koeber reaction (phenomenon)
- Auspitz sign: is pin point bleeding when a psoriatic scale is removed. (Severe thinning of the epidermis over the tips of dermal papillae)
- The psoriatic basal-cell is shed in about 4 days where as normal cell in 28 days
- The erythema is due to the dilatation & proliferation of the capillaries in the papillary dermis

Genetics and Pathogenesis

- Psoriasis and the Immune System
  - The major histocompatibility complex (MHC)
    - Short arm of chromosome 6
  - Histocompatibility Antigens (HLA)
    - HLA-Cw6
    - HLA-B13, -B17, -B37, -Bw16
  - T-lymphocyte-mediated mechanism

Triggering factors>

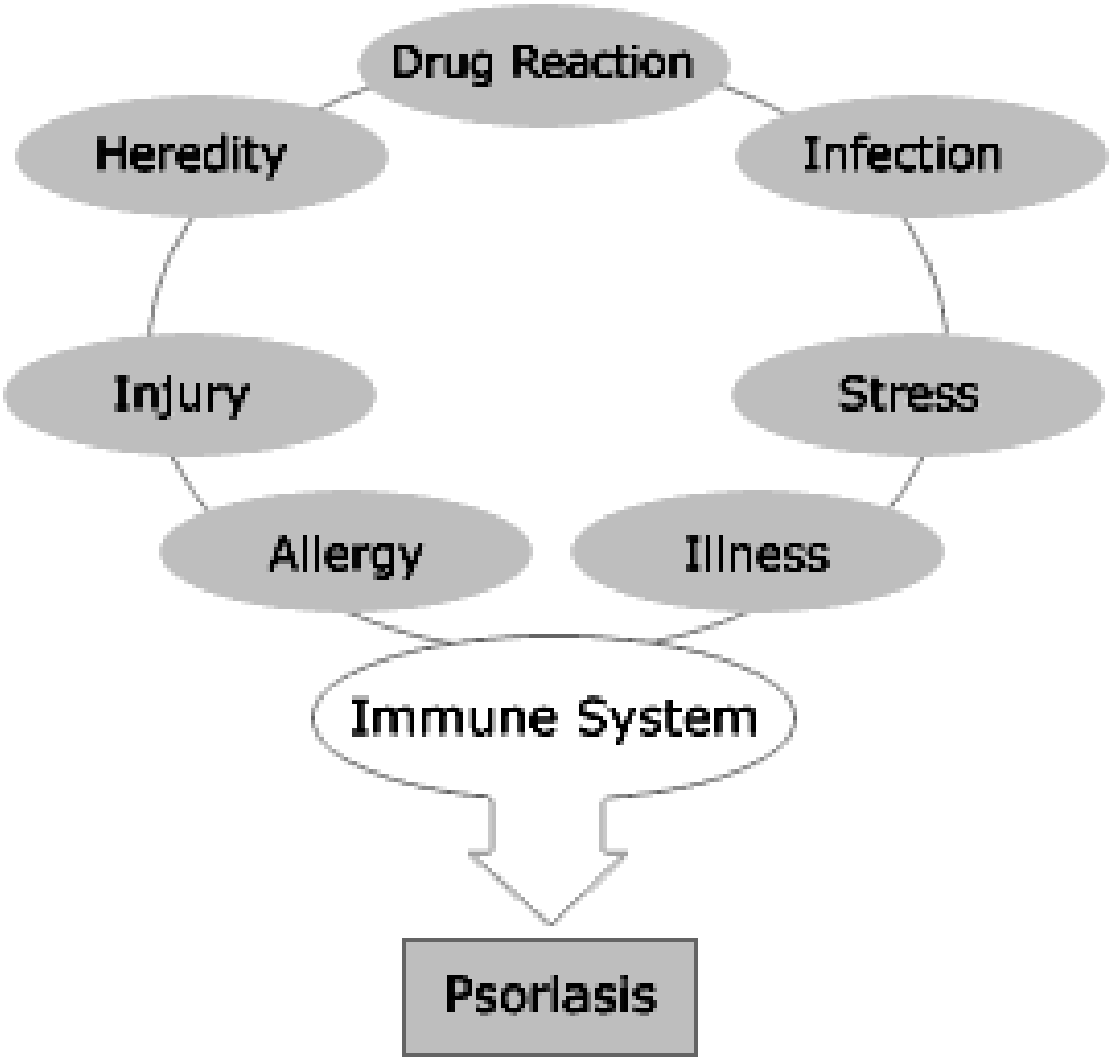
- Infections- streptococcal pharyngitis/tonsillitis

- Drugs- NSAID, beta blockers, lithium, antimalarials, corticosteroids

- Trauma- Koebner phenomenon

- Pregnancy
- Stress
- Alcohol
- Sunlight- worsening in ~10% of patients although majority beneficial to sun exposure

Psoriasis Triggers



Psoriasis : clinical features

- Well defined & circumscribed plaque
- Erythematous
- Silvery scaling
- Symmetrical
- Extensors of limbs, scalp, sacral area

❑ Auspitz's sign:

- light scraping of the scale with a wooden spatula produces multiple bleeding points
- extreme thinning of the epidermis over the capillary laden dermal papillae

Psoriasis as a Systemic Disease

- Koebner Phenomenon
- Elevated ESR
- Increased uric acid levels → gout
- Mild anemia
- Elevated α_2-macroglobulin
- Elevated IgA levels
- Increased quantities of Immune Complexes

Clinical Variants of Psoriasis

Clinical Types of Psoriasis

A. Non-pustular Psoriasis

B. Pustular Psoriasis

- **Localized**
- **Generalized**

C. Erythrodermic Psoriasis

D. Psoriatic arthritis

A. Non-pustular Psoriasis

- Chronic Plaque Psoriasis
- Regional Psoriasis
- Scalp Psoriasis
- Palmo-plantar Psoriasis
- Inverse Psoriasis (Flexural)
- Nail Psoriasis
- Guttate Psoriasis

Chronic Plaque Psoriasis

- ~80% of psoriasis
- Characteristic erythematous well defined circumscribed silvery scaly patches/ plaques
- Koebner phenomenon
    - Appearance of psoriasis in sites of skin trauma or pressure e.g. scratch marks, operation sites .
    - Present in lichen planus, vitiligo, viral wart
- “Atypical” with no scaling in moist flexural intertriginous area

Chronic Plaque Psoriasis

- Most Common Variant
- Plaques may be as large as 20 cm
- Symmetrical disease
- Sites of Predilection
  - Elbows
  - Knees
  - Presacrum
  - Scalp
  - Hands and Feet

Chronic Plaque Psoriasis

- May be widespread – up to 80% BSA
- Genitalia involved in up to 30% of patients
- Most patients have nail changes
  - Nail pitting
  - “Oil Spots”
  - Involvement of the entire nail bed
    - Onychodystrophy
    - Loss of nail plate

❑**Auspitz's sign:**

- light scraping of the scale with a wooden spatula produces multiple bleeding points
- extreme thinning of the epidermis over the capillary laden dermal papillae

Koebner phenomenon

- Appearance of psoriasis in sites of skin trauma or pressure e.g. scratch marks, operation sites .
- Present in : lichen planus, vitiligo, viral wart

Scalp Psoriasis

- Common
- Well demarcated erythematous silvery scaly plaque with normal skin intervening
- Post-auricular area commonly involved
- Non scarring alopecia when severe, regrow when condition improve
- DDx with seborrhoeic dermatitis by presence of typical plaque elsewhere +/- psoriatic nail changes

Palmoplantar Psoriasis

- Common
- Indurated heavily scaled plaque +/- fissuring
- Well-demarcated
- DDx with foot/ hand eczema

Nail Psoriasis

- ~50% of psoriasis have nail changes
- Pitting
- Onycholysis (separation of nail plate from nail bed)
- Oil drop sign (a yellow brown, subungual spot surrounded by erythema)
- Subungual hyperkeratosis
- Secondary onychomycosis is common

Guttate Psoriasis

- Latin “gutta” means a drop
- Mainly affects children and young adults
- Characterized by numerous 0.5 to 1.5 cm papules /plaques
- Very small plaques generalized with centripetal distribution
- May coalescent into larger plaques
- Preceded by streptococcal tonsillitis or pharyngitis 2 weeks before onset
- Spontaneous remissions in children
- Often chronic in adults

Flexural Psoriasis

- Psoriasis affecting axillae, perineum and umbilicus
- Atypical psoriasis as friction & humidity removes the scale (diagnostic confusion)
- Irritating when sweating

Life–Threatening Forms of Psoriasis

- Generalized Pustular Psoriasis
- Erythrodermic Psoriasis

Palmoplantar Pustular Psoriasis

- Relatively uncommon variant
- Painful, sterile pustules develop within plaque at palms and soles
- Pustules resolve to leave post inflammatory hyperpigmentation
- Female predominance
- 20% associated with psoriasis elsewhere
- Almost exclusively associated with smoking
- Resistant to topical treatment

Generalized Pustular Psoriasis

- Von Zumbusch's disease
- Erythematous edematous plaques studded with monomorphic sterile pustules. often after short episodes of fever of 39˚ to 40˚C
- Weight loss , Muscle Weakness, Hypocalcemia Leukocytosis , Elevated ESR
- Precipitated by :
- withdrawal of oral steroid or widespread use of ultra potent topical steroid
- pregnancy
- Can be life-threatening due to fluid loss, sepsis

Erythrodermic Ps.

- Universal redness & scaling
- Often nail & hair growth disturbance
- May be an end-result of acute Ps.
- Exfoliative Ps.
  - Unwell, fever, leucocytosis
  - Excessive of body heat & hypothermia
  - Inc. cut. blood flow ➡ high card. output ➡ heart failure
  - Inc. percutaneous loss of water ➡ Inc. loss of protein & iron (through scales) ➡ hypoproteinaemia & iron defficiency anaemia.
- Increase epidermal permeability ?? topical steroids

Erythrodermic Psoriasis

- >90% of BSA affected
- Life threatening with transcutaneous fluid loss, temperature dysregulation, sepsis, high output, cardiac failure
- Other DDx of erythroderma- atopic eczema, drug eruption , cutaneous T cell lymphoma, pityriasis rubra pilaris

Erythrodermic Psoriasis

- Triggering Factors
  - Systemic Infection
  - Withdrawal of high potency topical or oral steroids
  - Withdrawal of Methotrexate
  - Phototoxicity
  - Irritant contact dermatitis

Drug-provoked (Induced)psoriasis: Reported agent

MOST COMMONLY ASSOCIATED AGENTS

Beta blockers

Lithium

Antimalarial

Nonsteroidal Anti-Inflammatory Drugs

Psoriatic Arthritis

- ~10% of chronic plaque psoriasis
- Only ~15% of cases with skin and joint disease begin simultaneously
- ~60% of skin disease precedes arthritis
- ~25% of arthritis precedes skin disease
- Probably a positive correlation between severity of skin disease and arthritis developing
- Association: HLA B27: sacro-ileitis;
- B38 and DR7: peripheral arthritis;
- B39: all types;
- DR4: symmetrical arthritis

5 Types of Psoriatic Arthropathy

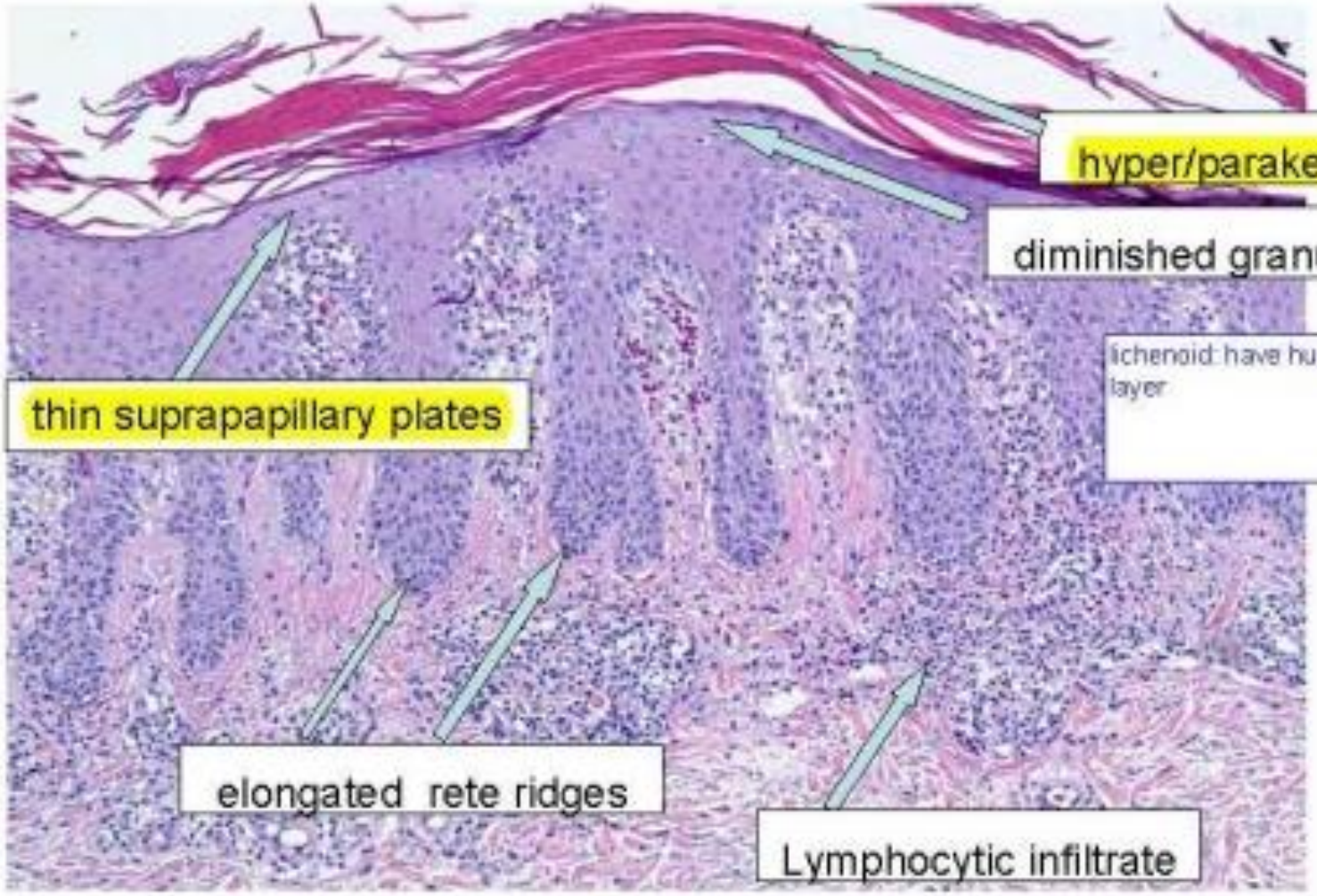
- Classical distal arthropathy-distal IP joint
- Seronegative RA-like polyarthritis
- Oligoarticular asymmetrical arthritis
- Spondyloarthropathy- Ankylosing spondylitis-like
- Arthritis mutilans

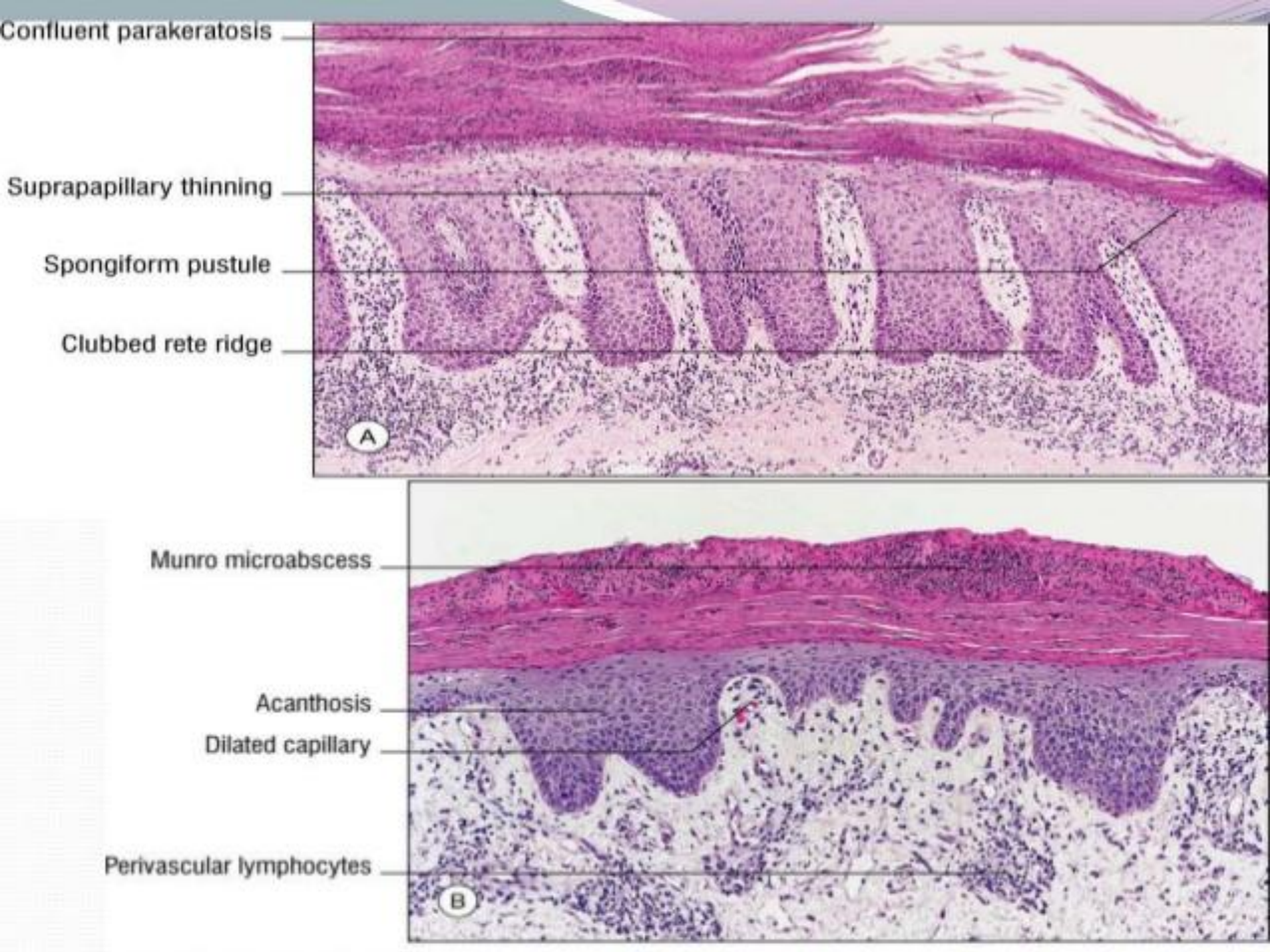
Psoriatic Arthritis treatment

- NASIDs- may exacerbate psoriasis
- Methotrexate
- Sulphasalazine
- Cyclosporine
- Systemic steroid- may make the skin lesions more difficult to control
- Biologics

Histopathological changes

- Inflammation
- Epidermal keratinocyte hyperproliferation
- (parakeratosis) incomplete cornification of keratinocytes with retention of nuclei
- (acanthosis), irregular thickening of the epidermis over the rete ridges but thinning over dermal papillae
- (munro abscesses) epidermal polymorphonuclear leucocyte infiltrates
- Vascular proliferation :dilated capillary loops in the dermal papillae


hyper/parakeratosis
diminished granular layer
lichenoid: have huge granular layer
thin suprapapillary plates
elongated rete ridges
Lymphocytic infiltrate


Confluent parakeratosis
Suprapapillary thinning
Spongiform pustule
Clubbed rete ridge
A
Munro microabscess
Acanthosis
Dilated capillary
Perivascular lymphocytes
B

Laboratory findings

- Elevated uric acid
- Mild anemia
- Negative nitrogen balance
- Increase sedimentation rate
- Increase alpha-2-microglobulin
- Incresae IgA and IgA immune complex

Differential diagnosis

Erythroderma

- Atopic dermatitis
- Sezary syndrome
- Drug eruption
- Generalized contact dermatitis

Intertrigenous psoriasis

- Candidiasis
- Contact dermatitis
- Darier’s disease

Differential diagnosis

Psoriasis vulgaris

- Nummular eczema
- Mycosis fungoides, plaque stage
- Tinea corporis

Guttate psoriasis

- Pityriasis rosea
- Pityriasis lichenoides et varioliformis
- Syphillis
- Tinea corporis

Differential diagnosis

Nail psoriasis

- Tinea ungium
- Dyskeratosis : secondary to injury

Scalp and face

- Seborrheic dermatitis

Genitalia

- In situ squamous cell CA

Current Treatment Approaches

Treatment Options

- Monotherapy
- Combination therapy
- Rotational therapy
- Sequential therapy

Treatment of Psoriasis

- What influences therapy choice?
  - Clinical type and severity of psoriasis (eg, mild vs moderate-to-severe), assessed by Psoriasis Area and Severity Index (PASI)
  - Response to previous treatment
  - Therapeutic options
  - Patient preference
- The "1-2-3" step approach is no longer generally accepted for disease more than mild in severity
  - Level 1: Topical agents—do not work
  - Level 2: "Phototherapy"—difficult; not always available
  - Level 3: Systemic therapy
- Risk in relation to benefit must be evaluated

Camisa C. *Cleve Clin J Med*. 2000;67:105-119.

Topical Agents

- Initial therapeutic choice for mild-to-moderate psoriasis
  - Emollients
  - Keratolytics (salicylic acid, lactic acid, urea)
  - Coal tar
  - Anthralin
  - Vitamin D_3 analogues (calcipotriene)
  - Corticosteroids
  - Retinoids (tazarotene, acitretin)
- Compliance can be difficult due to amount of time required to apply topicals 2 to 4 times/day

Camisa C. *Cleve Clin J Med.* 2000;67:105-119.

Systemic Therapy

- Systemic therapy should be reserved for patients with disabling psoriasis despite topical therapy
  - Psoralen + UVA light
  - Oral retinoids: acitretin (+/- phototherapy)
  - Methotrexate
  - Cyclosporine

Carrisa C. Cleve Clin J Med. 2000;67:105-119.

Phototherapy

- Used to treat moderate-to-severe psoriasis
- Phototherapy causes death of T cells in the skin
  - Natural sunlight
  - Ultraviolet (UV) B light
  - UVB light + coal tar (Goeckerman treatment)
    - Best therapeutic index for moderate-to-severe disease
  - UVB light + anthralin + coal tar (Ingram regimen)
  - Usually 3 treatments/week for 2 to 3 months is needed
  - Accessibility to a light box facility and compliance necessary

Carrisa C. *Cleve Clin J Med*. 2000;67:105-119.

UVA Light With Psoralen (PUVA)

- Psoralen is a drug that causes a toxic reaction to skin lymphocytes when it is activated by UVA light
- Psoralen can be given systemically or topically
- Effective treatment—longest remissions of any treatment available
- Adverse effects
  - Nausea, burning, pruritus
  - Risk of cancer with cumulative use—both squamous cell carcinoma and melanoma
    - >160 cumulative treatments

Greaves MW, et al. *N Engl J Med.* 1995;332:581-588.

Methotrexate

- Folic acid metabolite
  - Blocks deoxyribonucleic acid synthesis, inhibits cell proliferation
- Dose
  - Start at about 15 mg/week; maximum 30 mg/week
  - Can also be given intramuscularly
- Adverse effects
  - Headache, nausea, bone marrow suppression
  - Cumulative dose predictive of liver toxicity
    - Prospectively identify risk factors for liver disease
    - Guidelines recommend liver biopsy after 1.5 g
    - Teratogenic in men and women

Greaves MW, et al. *N Engl J Med.* 1995;332:581-588.

Acitretin: Oral Retinoid

- Frequently used in combination with topical agents, systemic therapies, and UV light
- Less effective as monotherapy for plaque psoriasis
- Plaque psoriasis dose
  - Start at 10 to 25 mg/day
- Adverse effects (fewest dose-related adverse effects)
  - Peeling/dry skin, alopecia, muscle pain
  - Lipid abnormalities
- Teratogenic: avoid pregnancy

Greaves MW, et al. *N Engl J Med.* 1995;332:581-588.

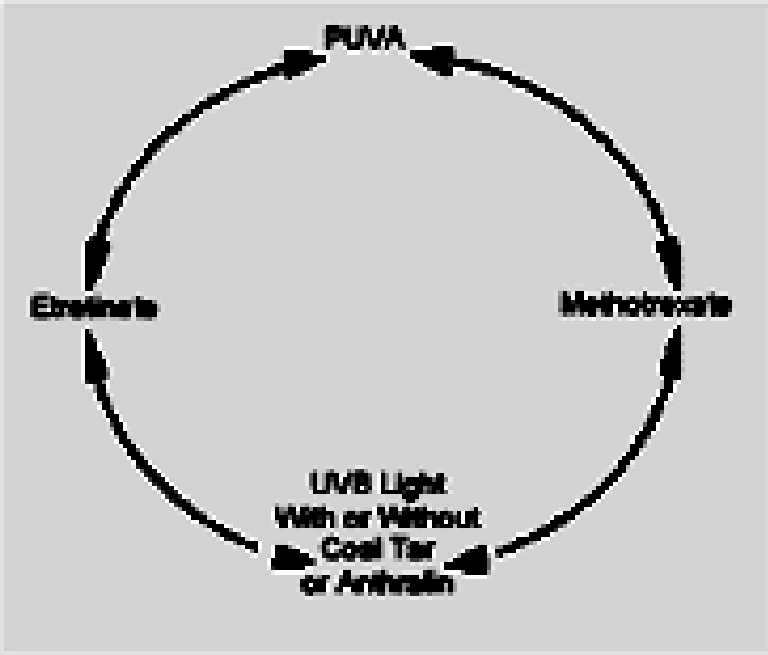
Cyclosporine

- Reserved for severe, recalcitrant disease
- Inhibits the proliferation of activated T cells
- Dose: 4 mg/kg/day, not to exceed 5 mg/kg/day
  - Tapering slowly may improve remission
- Use not recommended for >1 year
  - Renal toxicity
- Patients relapse 2 to 4 months after discontinuing
- Adverse effects
  - Immunosuppression: infections, possible malignancy
  - Hirsutism, gingival hyperplasia, muscle pain, infection
  - Serious: hypertension, renal failure

Lebwohl M, et al. *J Am Acad Dermatol*. 1998;39:484-475.

Rotational/Sequential Treatment

- Therapeutic strategy for moderate-to-severe disease
  - Switch to alternative therapy before early evidence of toxicity



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New Treatments

Biologic Therapies Currently Approved for the Treatment of Psoriasis

- Alefacept
- Efalizumab
- Etanercept

Systemic Treatment of Psoriasis

Currently licensed biologics for psoriasis

Type Drug	Route	Dosing	Freq PlasmaHalf-life
Adalimumab			
TNF-α inhibitor	Subcutaneous	80mg 1st week, then40mg 2nd wk ,ThenEvery 2 wk	2 weeks

Etanercept

Subcutaneous
50mg (0.8mg/kg, max 50mg)
First 12 week: twice a wk   Then once aweek
70 hours

Infliximab

IL-12/23Antibody
Intravenous
5mg/kg
0,2,6 wk, then every 8 wk8-9.
5days

Ustekinumab

Subcutaneous
45mg for <100 kg90mg for >100kg0,4 wk, thenevery 12 wk
15-32days

Absolute Contraindications:

- Pregnancy/breastfeeding
- Active (chronic) infections (including tuberculosis and active chronic hepatitis B)
- Congestive heart failure (NYHA grade III or IV)

Relative contraindications

- History of recurrent infections
- PUVA >200 treatments (especially if followed by cyclosporin use)
- HIV or AIDS
- Hepatitis C
- Congestive heart failure (NYHA grade I or II)
- SLE, Demyelinating disease
- Malignancies or lymphoproliferative disorders
- Live vaccines

Treatment Modalities:

- Combination therapy
  - -contraindicated in additive increase risk/ S/E, e.g.
  - Phototherapy +CsA increase risk of cutaneous cancer
  - Acitretin +MTX increase risk of hepatotoxicity

Treatment Modalities:

- Rotational therapy

  - use of therapies for a specified period (e.g.1-2 year) then rotate to an alternative therapy to minimize long-term toxicity in any given therapy and decrease therapy resistance/ tachyphylaxis

Treatment Modalities:

- Sequential therapy-

- Induction phase: use stronger potentially more toxic agents to clear psoriasis initially
- e.g. Ultrapotent topical steroid or CsA
- Transitional phase
- e.g. OM steroid+ Nocte calcipotriol or acitretin
- Maintenance phase: use of a “weaker”, less toxic agent for maintenance
- e.g. weekday calcipotriol +weekend steroid or acitretin +/-UVB/ PUVA

PITYRIASIS ROSEA

Pityriasis Rosea

Acute, self-limiting, mild inflammatory exanthem of unknown origin.

Etiology:

- Unknown
- A virus infection is most frequently suggested?
  - The formation of herald patch
  - The self-limited course
  - The seasonal preponderance & rare recurrence
- The Pit. rosea-like may occur as a reaction to:
  - Captopril
  - Gold
  - Clonidine
  - Barbiturates
  - Arsenicals
  - Bismuth
  - Methoxypromazine

Epidemiology:

In children and young adult
-Increased incidence in spring and autum
-PR has been estimated to account for 2% of dermatologic outpatient visits
-PR is more common in women than in men

Pathophysiology:

-PR considered to be a viral exanthem
-Immunologic data suggest a viral etiology
-Families and close contacts
-A single outbreak tends to elicit lifelong immunity
-Human herpesvirus (HHV)–7and HHV-6
-PR-like drug eruptions may be difficult to distinguish from non–drug-induced cases
-Captopril, metronidazole, isotretinoin, penicillamine, bismuth, gold, barbiturates, and omeprazole

- Begins with a solitary macule that heralds the eruption(herald spot/patch)
- Usually a salmon-colored macule
- 0ver a few days it become a patch with a collarette of fine scale just inside the well-demarcated border
- Within the next 1-2 weeks, a generalized exanthem usually appears
- Bilateral and symmetric macules with a collarette scale oriented with their long axes along cleavage lines
- Tends to resolve over the next 6 weeks
- Pruritus is common, usually of mild-to-moderate severity
- Over trunk and proximal limbs

Pityriasis Rosea

Clinical features

- Salmon-colored papular & macular lesions
- Oval patches or circinate covered with finely crinkled, dry epidermis ➡ often desquamates
- Usually begins with a single - herald or mother patch
- The new lesions spread rapidly
- Arranged - runs parallel to the lines of cleavage
- Generalized, affecting the trunk & sparing the sun-exposed surfaces
- Moderate pruritus may be present
- Variations in the mode of onset, course and clinical manifestations are common (papular Pit. Rosea)

oval

Atypial form of PR :

- **Occurs in 20% of patients**
- **Inverse PR**
- **Unilateral variant**
- **Papular PR**
- **Erythema multiforme–like**
- **Purpuric PR**

Differential Diagnosis :

Viral exantheme
Drug Eruption
Lichen Planus
Psoriasis, Guttate
Syphilis
Tine Corporis
Seborrheic Dermatitis
Nummular Dermatitis
Pityriasis Lichenoides

Pityriasis Rosea

Treatment

- Prevent irritable hot baths & soaps and woolen clothes
- Symptomatic
- Emollients
- Corticocosteroid (Topical, Oral, IM)
- UVB

Lichen planus (LP)

Background:

-Lichen planus (LP) is a pruritic, papular eruption characterized by its violaceous color; polygonal shape; and, sometimes, fine scale
-It is most commonly found on the flexor surfaces of the upper extremities, on the genitalia, and on the mucous membranes.

Lichen Planus & Lichenoid Eruption

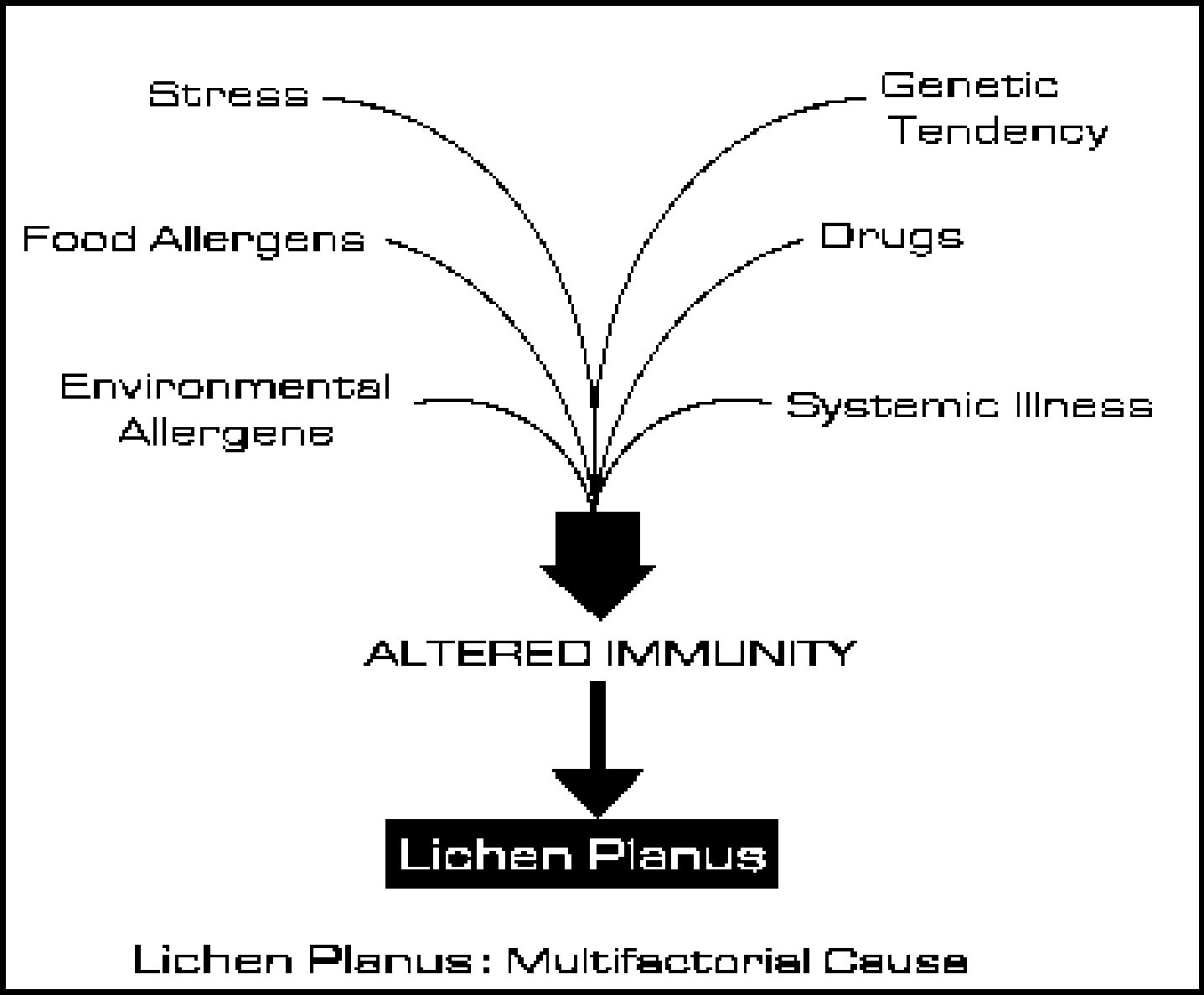
- Inflammatory pruritic disease of the skin and mucous membranes
- Rare in children
- Etiology:
  - The cause of LP remains unknown
  - ?? an alteration of epidermal cell antigens induce a cell mediated immune response
  - ?? may be familial (early age & chronic)
  - Drugs ➡ may induce lichenoid reactions (e.g. antimalarials, thiazide derivatives, propranolol..)
  - Viral infection? Symmetrically associated with viral hepatitis
  - A psychogenic origin? Severe psychic trauma
  - An auto-immune phenomenon?

Epidemiology :

-Approximately 1% of all new patients seen at health care clinics
-Rare in children
-F=M
-No racial predispositions have been noted
-LP can occur at any age but two thirds of patients are aged 30-60 years

Pathophysiology :

The cause of LP is unknown
-LP may be a cell-mediated immune response of unknown origin
-LP may be found with other diseases of altered immunity like ulcerative colitis, alopecia areata, vitiligo, dermatomyositis
-An association is noted between LP and hepatitis C virus infection ,chronic active hepatitis, and primary biliary cirrhosis
-Familial cases
-Drug may induce lichenoid reaction like thiazide,antimalarials,propranolol



Lichen Planus: Multifactorial Cause

Clinical Features :

Most cases are insidious
-The initial lesion is usually located on the flexor surface of the limbs
-After a week or more, a generalized eruption develops with maximal spreading within 2-16 weeks-
-Pruritus is common but varies in severity
-Deep pigmentations may persist for long time.
-Oral lesions may be asymptomatic or have a burning sensation
-In more than 50% of patients with cutaneous disease, the lesions resolve within 6 months, and 85% of cases subside within 18 months

- The papules are violaceous, shiny, and polygonal; varying in size from 1 mm to greater than 1 cm in diameter
- They can be discrete or arranged in groups of lines or Circles
- Characteristic fine, white lines, called Wickham stria, are often found on the papules
- Oral lesions are classified as reticular, plaquelike, atrophic, papular, erosive, and bullous
- Ulcerated oral lesions may have a higher incidence of malignant transformationO(the development of squamous cell carcinoma)
- Genital involvement is common in men with cutaneous disease
- Vulvar involvement can range from reticulate papules to severe erosions

- Wickham's striae:

  Grayish puncta or streaks which form a network on the surface of the papules (focal increase in thickness of granular layer & infiltrate)

- Koebner's isomorphic phenomenon:

  As in psoriasis by physical trauma (scratching) skin lesions are produced in the scratch marks identical to those already on the pat. skin.

- Pruritus:

  - It is intolerable in acute cases
  - Most pat. react by rubbing rather than scratching

Clinical types:

- ✓ **Hypertrophic LP**

  -These extremely pruritic lesions are most often found on the extensor surfaces of the lower extremities, especially around the ankles

- ✓ **Atrophic LP**

  -is characterized by a few lesions, which are often the resolution of annular or hypertrophic lesions

- ✓ **Erosive LP**

- ✓ **Folliculalar LP**

  -keratotic papules that may coalesce into plaques
  -A scarring alopecia may result

✓Annular LP

Annular lesions with an atrophic center can be found on the buccal mucosa and the male genitalia

✓Vesicular and bullous LP

-develop on the lower limbs or in the mouth from preexisting LP lesions

✓Actinic LP

-Africa, the Middle East, and India
-mildly pruritic eruption
-characterized by nummular patches with a hypopigmented zone surrounding a hyperpigmented center

✓LP pigmentosus

-common in persons with darker-pigmented skin
-usually appears on face and neck

LP and Nails

In 10% of patients
nail plate thinning causes longitudinal grooving and ridging
subungual hyperkeratosis, onycholysis
Rarely, the matrix can be permanently destroyed with prominent pterygium formation
twenty-nail dystrophy

Differential diagnosis

- Papular syphilis
- Guttate psoriasis
- Lichenoid forms of (eczema, scabies)
- Pityriasis rosea
- Leukoplakia (mucous m.)

Management :

self-limited disease that usually resolves within 8-12 months
-Anti-histamine
-topical steroids, particularly class I or II ointments
-systemic steroids for symptom control and possibly more rapid resolution
-Oral acitretin
-Photo-therapy
-Others


Thank you